ORIGINAL ARTICLE

Pregnancy Outcome in Women with Prosthetic Heart Valves

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ABSTRACT

Objective: To investigate the outcomes of pregnancy and delivery in patients with prosthetic heart valves as well as to assess the fetal and neonatal outcomes.
Study design: Descriptive observational study.
Place & duration of study: The Gynaecology & Obstetrics Department of Armed Forces Institute of Cardiology Rawalpindi from August 2009-January 2012.
Material and methods: 38 pregnancies with prosthetic heart valves were selected according to inclusion / exclusion criteria by convenience sampling. Detailed counselling and individualized decision making was carried out and they were divided among three groups according to the different anticoagulation regimes. Relevant data was obtained and outcomes of pregnancy like miscarriages, termination of pregnancy, type of delivery, adverse haemodynamic events during pregnancy, labour or puerperium, maternal deaths and fetal and neonatal outcomes were studied.
Results: We had metallic valves inserted in 34/38(89.47%) of the pregnancies and bioprosthetic valves in 4/38(10.52%). Mean age and parity were27.95±4.32 years and 1.74±1.23 respectively. Fetal attrition occurred in3/38(7.89%), 3/38(7.89%) and 1/38(2.63%) in the first, second and the third trimester respectively. We had 5/31(16.12%) premature births, Caesarean section in 13/31(41.93%) and 18/31(58.06%) vaginal deliveries. Adverse haemodynamic events and maternal deaths occurred in6/38 (15.78%) and 4/38 (10.52%) of pregnancies respectively, mostly in the groups 1 and 3. We had a generally good neonatal outcome with no case of warfarin embryopathy.
Conclusion: There was generally good maternal and neonatal outcome in patients with good NYHA functional class. Warfarin may be continued throughout pregnancy for these patients. Maternal deaths and adverse haemodynamic events could be reduced by better education, counselling and compliance with care
Key words: Prosthetic heart valves, anti coagulation, outcome, warfarin, pregnancy.

INTRODUCTION

The first successful replacement of heart valve in human was reported in1960. Since then prosthetic heart valves have been implanted in patients with both congenital and acquired valvular disease. Many of the recipients of such valves are women of child bearing age who desire to have children[1]. The management of pregnant women with such prosthesis is complicated and challenging because of difficulty in balancing maternal and fetal outcomes[2].

These replacements may be mechanical or bio prosthetic (heterografts or homografts). Mechanical valves are associated with an increased incidence of thrombo embolic events during pregnancy requiring therapeutic anticoagulation throughout pregnancy[3] along with risks of anticoagulation to the fetus, neonate and the mother. They have excellent durability and structural valve deterioration does not occur. In addition newer generation mechanical valves have superior hemodynamic profiles but require lifelong anticoagulation to prevent thrombo embolic complications which include stroke, valve thrombosis and myocardial infarction[4]. The main issues with bioprosthetic valves are their finite life span, risk of structural valve deterioration and need for re-operation[4]. These valves degenerate more quickly in younger patients, a process that can be further accelerated during pregnancy. Such patients may not require long term anticoagulation[1] and have been found to have excellent fetal outcomes[5]. Women who have well functioning bioprosthetic valves and who do not have other cardiac risk factors often have uncomplicated pregnancies[6]. Women with mechanical valves have higher incidence of pregnancy loss, premature births, maternal deaths, thrombo embolic complications and bleeding[5].

Sufficient anticoagulation after mechanical heart valve replacement is mandatory to prevent thrombo embolic complications. Pregnant women represent a special problem due to the hyper coagulable state during pregnancy and lack of reliable data on safety and efficacy of different anti coagulation regimes during pregnancy. Both Coumadin derivatives and heparin (low molecular weight heparin or clexane and

unfractionated heparin or uFH) for anti coagulation carry hazards during pregnancy, but whereas coumarins bring a small risk to the fetus of warfarin embryopathy; heparins jeopardize the mother by insufficient anti coagulation[7]. Anti coagulation management in pregnancy requires close collaboration between cardiologist and obstetrician and a thorough discussion of the risks and benefits of various anti coagulation regimes with the patient.

The optimal anti coagulation strategy in the pre pregnancy period and during pregnancy is controversial and a matter of debate. Recently a number of studies have evaluated therapeutic and management strategies for pregnancy and delivery in patients with prosthetic heart valves. However such strategies are often based on clinical assessments, small studies or case reports without clear data due to the non availability of standardized management and limited scientific evidence. Therefore currently it is impossible to provide evidence based recommendations about the risks of pregnancy or to optimize the management of such patients.The purpose of this study was to investigate the outcomes of pregnancy and delivery in patients with prosthetic heart valves as well as to assess the fetal and neonatal outcomes according to gestational age, apgar scores, birth weights, possible congenital heart disease ,signs of warfarin embryopathy and complications of anti coagulation.

MATERIAL AND METHODS

This prospective study was conducted from August 2009 to January 2012 at the Obstetrics & Gynaecology Department of Armed Forces Institute of Cardiology Rawalpindi, which is a tertiary referral centre for all cardiac patients. A total of 38 pregnancies were studied. All patients with either bioprosthetic or mechanical heart valves were included .Patients with other forms of heart lesions corrected by surgery or other valvular repair procedures were excluded from the study. Joint care by a multi disciplinary team including a cardiologist, obstetrician, paediatrician and an anaesthetist was provided to all the patients. Pregnancy was generally monitored according to the guidelines of the Task Force on the management of cardio vascular diseases during pregnancy of the European Society of Cardiology[8]. Patients underwent detailed counselling at the initial visit and subsequently as required regarding the risks and complications of pregnancy and anti coagulation and a detailed individualized decision making was done. Patients were divided into three groups based on their anti coagulation regime and the timing of the first visit. Group 1 comprised of patients who presented early in pregnancy and were receiving warfarin before pregnancy. They were started inj Clexane sub cutaneously in therapeutic doses from 6 to 12 weeks, again shifting to warfarin for the rest of the pregnancy till 36 weeks; whereby intra venous uFH was given after admission till the onset of labour. Group 2 included patients who reported late after the first trimester and were continued on warfarin throughout pregnancy till 36 weeks when it was substituted by uFH as mentioned before. In Group 3, the patients were not on anti coagulation during pregnancy although post delivery uFH or clexane may be used according to the risk factors. Patients on warfarin were monitored by INR (International normalized ratio)between 2-3, and those on uFH by daily PTTK levels between 1.5-2. All relevant data were obtained regarding patient's age, parity, gestational age, clinical presentation, New York Heart Association (NYHA) functional class[9], necessary investigations, comprehensive cardiac assessment and type of the valve replaced. Outcomes of pregnancy like miscarriages, termination of pregnancy, type of delivery, adverse haemodynamic events during pregnancy, labour or puerperium and maternal deaths were also recorded. Fetal and neonatal outcomes like early and late fetal attrition, prematurity, birth weight, apgar scores, congenital cardiac anomaly, signs of warfarin embryopathy and complications of anti coagulation were also recorded on a pre designed proforma.

Patients had anomaly scan and fetal echo cardiography arranged between 22-24 weeks. Patients in group 1 and 2 were routinely admitted at 36 weeks to arrange the shift over from warfarin to heparin and bishop's score was assessed on weekly basis. If bishop's score was good they were induced at 38 weeks; otherwise they were allowed to reach 40 weeks when induction of labour was planned. Those with failed induction of labour underwent caesarean section. Elective caesarean was planned at 37-38 weeks as required. All patients undergoing caesarean section, induction of labour or spontaneous labour were put on prophylactic antibiotics with a third generation cephalosporin. Unfractionated heparin was stopped at the onset of labour or four hours before caesarean and started again six hours after delivery or caesarean section. Those taking long term anti coagulation were shifted to warfarin after 2-3 days. All neonates were examined by a paediatrician. Mothers and neonates were discharged when they were stable.

The acquired data was analyzed using SPSS V16. Frequencies and percentages were used to describe the data. Means and standard deviation were calculated for maternal age, parity, neonatal birth weight and Apgar scores.

RESULTS

The study included 38 pregnancies with prosthetic heart valves. The baseline characteristics of these pregnancies are given in the Table-1. We had metallic valves inserted in 34/38(89.47%)of the pregnancies and bioprosthetic valves in 4/38(10.52%) of the pregnancies. 9/38 (23.68%) pregnancies had a double valve (aortic and mitral) replacement done, while 4/38 (10.5%) had aortic and 25/38 (65.78%) had mitral valve replacement done. We had 34/38 (89.47%) pregnancies in NYHA functional class 1, one (2.63%) in class 2 ,and three (7.89%) in class 4. There were seven (18.42%)patients on cardiac medications with two maternal deaths in this category.

Table 1: Characteristics of study population

Characteristic	**Group-1 (n=28)**	**Group-2 (n=5)**	**Group-3 (n=5)**
Mean age (yrs)	27.55±4.64	29.80±3.49	29.67±0.58
Mean parity	1.77±1.4	1.8±0.84	1.5±0.7
Type of valve replaced			
Metallic	28(73.68%)	5(13.15%)	1(2.63%)
Bioprosthetic	-	-	4(10.5%)
Location of the Valves Replaced			
DVR	7(18.42%)	2(5.26%)	-
AVR	3(7.89%)	1(2.6%)	-
MVR	18(47.36%)	2(5.26%)	5(13.15%)
NYHA Classes			
1-2	27(71.05%)	5(13.15%)	3(7.89%)
3-4	1(2.63%)	-	2(5.26%)

Table-2 Maternal outcomes

	Group-1 (n=28)	**Group-2 (n=5)**	**Group-3 (n=5)**
1st Trimester spontaneous miscarriage	2(5.26%)	1(2.63%)	--
Second trimester fetal loss	3(7.89%)	-	-
Third trimester fetal loss	-	-	1(2.63%)
Induction of labour(13/31)	10(32.25%)	2(6.45%)	1(3.22%)
Deliveries (n=31)	23(74.19%)	4(12.9%)	4(12.9%)
Vaginal delivery	13(41.93%)	3(9.67%)	2(6.45%)
Caesarean delivery	10(32.25%)	1(3.22%)	2(6.45%)
Undelivered	-	-	1/38
Adverse haemodynamic events	4/38(10.5%)	-	2(5.26%)
Maternal deaths	2(5.26%)	-	2(5.26%)

Table-3 Neonatal Outcomes

	Group-1 (n=28)	**Group-2 (n=5)**	**Group-3 (n=5)**
Mean birth weight (kgms)	2.82±0.61	2.64±0.32	3.13±0.47
Mean apgar score	8.32±0.73	8.48±0.71	8.71±0.63
Newborns(n=31)			
Premature	3(9.67%)	1(3.22%)	1(3.22%)
Full term	21(67.74%)	3(9.67%)	2(6.45%)
Neonatal deaths	2(6.45%)	1(3.22%)	-
Neonatal complications	3(9.67%)	-	-
Warfarin embryopathy	-	-	-

In group 1, 2 and 3 we had 28, 5 and 5 pregnancies respectively. Mean ages were 27.55±4.64, 29.8±3.49 and 29.67±0.58 years; while mean parity was1.77±1.4, 1.8±0.84 and 1.5±0.7 respectively in the three groups. First trimester spontaneous miscarriages occurred in 3/38 (7.89%) pregnancies. Fetal attrition in the second trimester included 3/38 (7.89%) pregnancies with two intra uterine deaths at 22 and 24 weeks gestation and one termination at 24weeks. Termination of pregnancy was carried out in this patient due to fetal abnormality (Dandy Walker Syndrome).We had a patient with pre mature pre term rupture of membranes with severe oligohydramnios at 27 weeks with neonatal death after vaginal delivery. We had one patient with intra uterine fetal death in the third trimester at 30 weeks with thrombosed mitral valve and heart failure who died in the emergency room with the fetus in utero. Another termination of pregnancy was done by emergency hysterotomy in a patient at 30 weeks gestation for recurrent fits due to cerebovascular bleed resulting in neonatal death due to respiratory distress syndrome. Group wise data of fetal attrition is given in Table 2. We had 31 deliveries in total, of which 26 /31(83.87%) were term deliveries and 5/31 (16.12%) delivered prematurely. Caesarean section was done in 13/31 (41.9%) pregnancies while vaginal delivery was contemplated in 18/31 (58.06%) of pregnancies. There was no assisted vaginal delivery. Induction of labour was done in 13/31 (41.9%) pregnancies; whereby nine delivered vaginally and the rest ended up in caesarean section.

Adverse haemodynamic events occurred in 6/38 (15.78%) of total pregnancies with 4/38(10.5%) in group 1 and 2/38(5.26%) in group 3. Maternal deaths occurred in 4/38 (10.5%) of total pregnancies with 2/38 (5.26%) in group 1 and 2/38(5.26%) in group 3. There were no adverse haemodynamic events or maternal deaths in group 2 which was a significant finding. One patient in group1 with previous history of cerebrovascular accident (CVA) developed CVA with

recurrent fits at 30 weeks in the present pregnancy as mentioned above. Femoral artery thrombosis occurred in a patient in group1 at 8 weeks gestation who was on clexane at that time. Surgical thrombolectomy was done and warfarin was restarted. She delivered a healthy baby by caesarean at 36 weeks. Another patient in group 1 with double valve replacement developed dilated cardiomyopathy with ejection fraction of only 15%. Emergency caesarean was done at 36 weeks but the patient died of atrial fibrillation the same day. We witnessed the sad demise of a young unbooked patient with thrombosed metallic mitral valve who landed in emergency with an intra uterine death of fetus. She was on warfarin for many years but left it during pregnancy and belonged to a far flung area and very poor social class. We admitted another patient with a double valve replacement in heart failure at 36 weeks. She had developed Tricuspid regurgitation with Pulmonary Hypertension and Dilated Cardiomyopathy. Warfarin was stopped and caesarean section was done after three days under cover of fresh frozen plasma and blood. She had severe chest pain with haemoperitoneum on the third post operative day for which she underwent a laparotomy.She remained well for two weeks when she developed sudden cardio pulmonary collapse secondary to right heart failure and died in spite of all resuscitative efforts. Another case of maternal mortality occurred in a stable obese patient with a bioprosthetic mitral valve replacement and mild mitral regurgitation. Caesarean section was done for failed induction and previous caesarean. She was not on any anti coagulation during pregnancy but was put on clexane for two weeks post operatively due to her obesity and discharged routinely. She died suddenly at home two weeks after caesarean. The exact cause of death could not be ascertained, although pulmonary embolism could not be ruled out from her presentation at death.

We had good neonatal outcome in patients with stable cardiac condition and in NYHA category 1 and 2. Mean birth weight of the neonates was 2.84±0.64 kgms. Mean Apgar score was 8.39±0.73. Neonatal adverse events occurred in 3/31, (9.67%) of neonates. Cephal haematoma occurred in one neonate whose mother presented in advanced labour with breech presentation while still therapeutically anti coagulated on warfarin at 36 weeks. The baby survived and recovered fully. Another full term neonate developed intra cranial haemorrhage and required neonatal intensive care admission. His mother was a primigravida and reported in labour while being therapeutically anticoagulated with warfarin. The baby made a good recovery and was discharged on tenth day with no residual disability at six months follow up. We had one neonatal death because of respiratory distress syndrome secondary to prematurity at 30 weeks. We had no case of warfarin embryopathy or congenital cardiac defects among the neonates.

DISCUSSION

The management of pregnant women with prosthetic heart valves still raises important concerns and unresolved questions. Such pregnancies present a challenge to the obstetricians caring for both the mother and the fetus .In our study most women had metallic heart valve replacements and good NYHA functional class. These women had generally a good maternal and neonatal outcome. However adverse haemodynamic events were not uncommon. These events were much lower than the 27% reported in some earlier studies[10]. The occurrence of cerebrovascular haemorrhage and haemoperitoneum were the two incidences of haemorrhagic complications2/38 (5.26%) in our study. There was no case of excessive post partum vaginal bleeding. This very low incidence of post partum haemorrhage (PPH) can be compared with study by Matoras[11] who had only one case of PPH in 59 deliveries in patients on oral anti coagulant therapy. In a systematic review by Chan and colleagues, the overall rate of major bleeding in pregnancy with mechanical heart valves was reported to be 2.5%[12]. The occurrence of femoral artery thrombosis in one patient while on LMWH suggests it may not be as effective in preventing thrombosis as warfarin and patients having high risk of thrombosis should continue with oral warfarin throughout pregnancy. Ahmed Hassouna[13] determined a four times elevated rates of thromboembolic complications and mortality with heparin therapy as compared to oral anticoagulation. Salazar[14] reported three cases of valvular thrombosis and fourteen cases of cerebral embolism in his study. On the contrary we had no case of valve thrombosis in patients receiving warfarin, while the single case of valve thrombosis occurred in a patient not taking any anti coagulation.

Maternal mortality remains the most devastating complication and many case series confirm that mortality and near misses cannot necessarily be avoided[15,16] . The overall mortality in our study was 4/38(10.52 %) which was higher as compared to the study in Denmark[17] of 3.3%. This difference could be explained in part due to the lack of education, almost non existent pre pregnancy counselling ,failure to adhere to timely ante natal care schedule and non compliance with medications in our patients. Almost half of the mortalities in our study could have been avoided. Failure to stop warfarin in time at 36 weeks

gestation, development of haemoperitoneum and re laparotomy in an already compromised patient in one instance and failure to take warfarin in pregnancy resulting in thrombosed mitral valve in the other were avoidable causes of death. The mortality rate in our patients is much higher when compared to the general population in Pakistan[18]. However simply comparing mortality in this patient group with healthy pregnant women may not be appropriate as young patients with significant cardiac problems per se will have higher mortality rates irrespective of pregnancy and anti coagulation[19].

The rate of spontaneous miscarriage in our patients was 7.89 % which was lower than that reported by Chan et al[12] and Mihaljevic[20], while fetal attrition in the second trimester was higher in our study. However earlier studies[12] have failed to link any specific anti coagulant strategy with a particularly high miscarriage rate but recent experience with LMWH indicates that this problem can be avoided by its use[16] as clearly depicted in our study.

We had a caesarean section rate of41.9% and induction of labour in 41.9 %. This was lower than the 55% caesarean section rate in Denmark as given by Martin Sillesen et al[17]. We had a lower rate because it was reserved for obstetric indications and emergency situations only and the availability of centralized and highly specialized care by multi disciplinary team. We had a high induction of labour rate owing to the fact that once warfarin is stopped at 36 weeks, the prolongation of pregnancy for more than three weeks increases the danger of thrombosis in patients maintained on intra venous heparin.

The generally good neonatal outcome in our study could be attributed to the good NYHA functional class and the corrected nature of valvular lesions. There was no case of warfarin embryopathy in our neonates. This result was similar to other studies by Voral et al[21], Geelani et al[22] and Al Lawati[23]. Therefore it may be suggested that the teratogenic effects of warfarin during the first trimester may have been over estimated. However, further large trials are needed to confirm this suggestion. Even the neonates who developed short term complications of anti coagulation like cephal haematoma and intra cranial haemorrhage recovered very well and had no long term residual effects. The rate of healthy neonates born to these mothers was 28/31(90.3%) which was higher than that found by Nassar et al[24] and Kim et al[25].

CONCLUSION

Patients with mechanical heart valves need an enhanced level of medical care during pregnancy and puerperium.There were generally good maternal and neonatal outcomes in patients with good NYHA functional class and stable cardiac condition. Considering the low socio economic class, resource poor settings and the low risk of warfarin embryopathy, we conclude that warfarin may be continued throughout pregnancy for these patients. Maternal deaths and adverse haemodynamic events could be reduced if patients are better educated, counselled and compliant with preconception and ante natal care.

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